June 8, 1956

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Copenhagen S, Denmark

Dear colleagues:

I am sorry to be so tardy in discussing some preliminary research plans, and I hope it will not be too late for you to do some exploratory work this summer. Don't fret about it if you are too busy with other matters.

We will have ample opportunity to discuss further details, but there are three closely related problems that occur to me as very pertinent to your existing facilities and specialties: 1) immunogenetics of O,K,H antigens in crosses; 2) a study to determine whether "F" can be characterized serologically; 3) a survey of E. coli strains for lysogenicity to determine whether other interesting transduction systems can be found. For the easiest approach to these problems, the calculated choice of strains is of the utmost importance, and I have hoped you would be able to use some of your present facilities this summer in a preliminary way.

For 1), I still believe it would be most useful to use the K_B types, particularly because of their epidemiological importance, and the question whether the O and B antigens can be separated. We have had some frustrations in past work with such types, but I believe we should screen as many additional strains (of independent origin) as possible. The screening would best be done here, but I suggest that you collect as large a variety of isolates as you can and bring them with you. It would also be advantageous if you could bring your own sera for the characteristic antigens of these types.

2) It would be extremely interesting, and possibly very useful for further study of sexual compatibility, if F+ could be differentiated from F- strains on a serological basis. Here, unfortunately, K-12 appears to be useless owing to its auto-agglutinability and lack of complete antigen. We have made a preliminary study on serotype and on mating behavior of a number of other strains. I am sending you the following with the request that you give them a more than routine serological diagnosis in so far as this is possible (some of them are doubtless rough). What would be most useful would be a pair of strains from this group which are both antigenically complete, but which behave the most "cleanly" with regard to the separation of O, K and H reactions, and to the minimization of cross reactions between them. Most of the strains in this list are now F- but can be converted to F+ by exposure to other F+ strains. If the right pair of strains can be found, it would greatly simplify attempts to distinguish F+ from F-, and to demonstrate that different serotypes develop a common reactant when they are made F+. As the extent to which these strains has been studied is very variable, both genetically and serologically, please keep me informed of your findings so that you do not exaggerate your effort on some strains which may be genetically less well known than others. Some of these strains may also be useful for problem 1.

3) For this purpose I am sending you W-3001 as an indicator. This is a

lambda-sensitive, streptomycin-resistant mutant of E. coli K-12. [Although K-12 has been studied before with not very staisfactory results, I would ask you to see what you can do about the serotype (at least for H antigens) of this strain]. You doubtless have your own techniques that you may wish to follow in screening for lysogenicity, and I would also encourage you to use other indicators (e.g., a rough Shigella dysenteriae which has been found to be sensitive to a great many phages carried by coli strains); I might suggest the following: grow W-3001 together with the proband strain in broth, then spot the mixed culture on a lawn of W-3001 on a streptomycin medium. If you have already collected any variety of phages from lysogenic bacteria (of any type) which are active on E. coli, I would be interested to hear of it. I should simply suggest that some few hundreds of miscellaneous strains be tested in this fashion.

Besides W-3001, I am sending the following under separate cover:

WG-3
-4
19
28 = NCTC 123
(special question: are 28, 28A,51 distinguishable)
28A serologically
33
37
39
40
43
46
47
48
51 = NCTC 122
52 = Kauffmann O 18
53 20
54 21
55 25
56 026 B6 H?
57 055 B5 H?

15
16
24
26

If this is too long a list let me know, and I will try to be more discriminating.

We will be away from Madison for brief intervals, and this may account for possible delays in reply to your correspondence. However, we will be here for most of the summer.

If there is anything further I can do here to smooth your path, let me know.

Sincerely,

Joshua Lederberg